EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201402023

Iron-Catalyzed Arylation of Aromatic Ketones and Aldehydes Mediated by Organosilanes

Risto Savela,[a] Marcin Majewski,[a] and Reko Leino*[a]

Keywords: Synthetic methods / Homogeneous catalysis / Iron / Silanes

A simple and efficient iron-catalyzed method for arylation of aromatic carbonyl compounds is reported. The use of 4 % $FeCl_3$ or $Fe(acac)_3$ as the catalyst, in combination with a slight excess of chlorotrimethylsilane and triethylsilane, chlorination of benzylic ketones and aldehydes with subsequent Friedel–Crafts alkylation of arenes is achieved. Although the method is limited by the general constraints associated with Friedel–Crafts alkylation reactions, robust applications for the synthesis of pharmaceutical intermediates and so on can be envisioned.

Introduction

The field of iron-catalyzed transformations has rapidly expanded in the past decade.[1] For example, iron-catalyzed reductions of organic compounds with organosilanes as the hydride source have been widely investigated.[2] Typically, carbonyl compounds are reduced to alcohols by hydrosilylation followed by subsequent quenching.[3] Reductions of nitriles, amides and imines to amines have likewise been reported.[4] Also recently, iron-catalyzed reductions of sulfoxides[5] to sulfides, as well as chemo-, regio- and stereoselective hydrosilylations of alkenes and alkynes[6] have been investigated. Furthermore, deoxygenative transformations of silyl ethers to chlorides[7] and azides[8] and preparations of ethers through condensation reactions of ketones, aldehydes or alcohols,[9] and through reduction of esters[10] have been described.

Friedel–Crafts-type reactions, in general, have significant applications in both laboratory and industrial synthesis with the Friedel–Crafts benzylation being one of the fundamental methods used for preparation of diarylalkanes, which, in turn, are useful intermediates for dyes, pharmaceuticals and cosmetics.[11] Representative examples of pharmaceutical targets that could be obtained by Friedel–Crafts chemistry are shown in Figure 1. Although the direct use of carbonyl compounds as alkylating agents in Friedel–Crafts alkylations is attractive (Scheme 1), such reactions often suffer from low yields and undesirable side-product formation as a result of multiple alkylations.[12] Acid-catalyzed reductive Friedel–Crafts reaction between benzaldehyde and benzene has been known since 1886,[13] typically to yield a mixture of products in low yields.[14] Since then, the field of catalytic benzylations has expanded remarkably. In recent investigations, the frequent use of benzylating agents have included acetylated or trimethylsilylated benzylic alcohols,[15] styrene derivatives,[16] benzyl alcohols[17] and benzyl thiocyanates.[18]

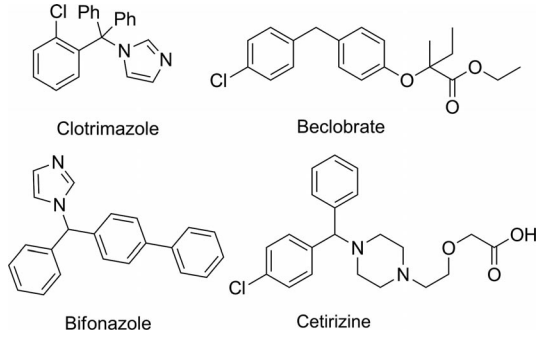
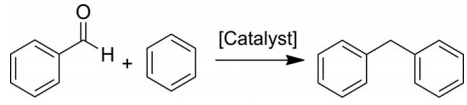


Figure 1. Representative examples of pharmaceuticals with precursors obtained thorugh Friedel–Crafts alkylation.



Scheme 1. Reductive Friedel–Crafts alkylation.

One of the first examples of catalytic reductive Friedel–Crafts alkylations utilized Ga_2Cl_4,[19] with subsequent reports on the use of superacid,[20] and scandium(III) trifluoromethanesulfonate as the catalysts.[21] Other earlier reported approaches have involved the use of $InCl_3$[22] and $InBr_3$[23] together with chlorodimethylsilane. Iron-catalyzed Friedel–Crafts reactions with $FeCl_3$ in the presence of chlorodimethylsilane and thiophene as the nucleophile have also been reported.[24] In our ongoing search for applications of economically viable iron catalysts, in particular $FeCl_3$,[25] we turned our attention to its potential use in re-

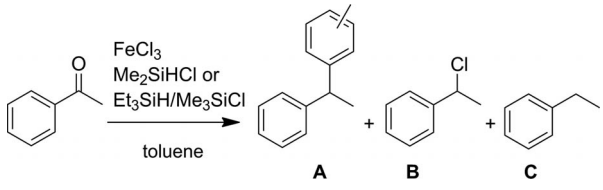
[a] Laboratory of Organic Chemistry Åbo Akademi University, 20500 Åbo, Finland
E-mail: reko.leino@abo.fi
http://www.abo.fi/rlgroup

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201402023.

ductive Friedel–Crafts alkylation reactions in combination with organic silanes. Here, we report the initial results of our investigation.

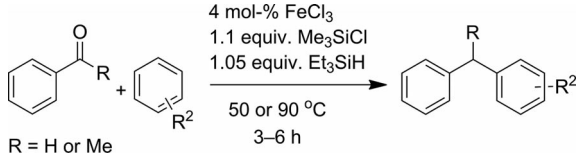
Results and Discussion

The aim of the present work was to investigate the use of $FeCl_3$ as the catalyst, in combination with organosilanes, for Friedel–Crafts-type alkylation reactions of aromatic ketones and aldehydes. In the preliminary experiments, acetophenone was reacted in an excess of toluene with $FeCl_3$ as the catalyst in the presence of chlorodimethylsilane (Scheme 2). In contrast to literature precedence,[24] instead of desired diarylethane **A**, corresponding reduced ethylbenzene **C** was primarily formed. The selectivity could, however, be reversed by addition of the organosilane as a dilute solution by means of a syringe pump. Although promising at first, this approach proved problematic and resulted in extensive formation of acyclic and cyclic polydimethylsiloxane byproducts, causing purification problems on the preparative scale. Finally, the selectivity issues were resolved by switching to the use of chlorotrimethylsilane as the chlorine source, followed by portionwise addition of a diluted triethylsilane solution at room temperature. By using this methodology, formation of corresponding 1-chloro-1-phenylethane **B** intermediate was observed with concomitant suppression of the formation of undesired polysiloxane byproducts. Instead, only easily separable hexaethyldisiloxane and 1,1,1-triethyl-3,3,3-trimethyldisiloxane compounds were formed as side-products. Earlier, a similar approach for chlorination of carbonyl compounds by using $In(OH)_3$ as the catalyst, in combination with chlorodimethylsilane as both the chlorine and hydride source, has been reported.[26] The yields obtained were better than the combined use of chlorotrimethylsilane and triethylsilane.[26]



Scheme 2. Initially investigated catalyst system for the Friedel–Crafts arylation reaction.

Under the reaction conditions screened in the present work, the desired Friedel–Crafts alkylation took place at elevated temperatures 50–90 °C. The general, optimized catalyst system used for substrate scope investigation is illustrated in Scheme 3 with results on the cascade-type chlorination Friedel–Crafts alkylation reaction sequence of benzylic ketones collected in Table 1 and the corresponding reactions with benzaldehydes as the electrophile shown in Table 2. For some starting materials further adjustments were necessary to suppress the potential side reactions, optimize the reaction yields and to isolate the final products. Ideally, the arene reagents studied were also used as solvents.

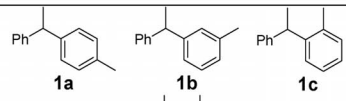
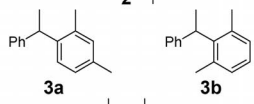
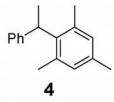
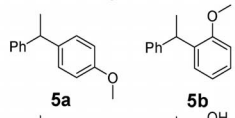
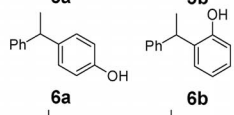
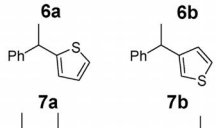
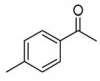
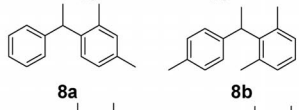
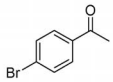
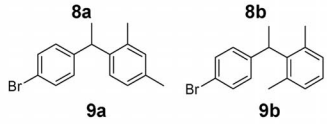
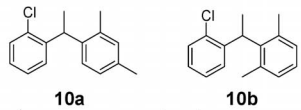
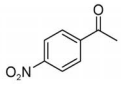
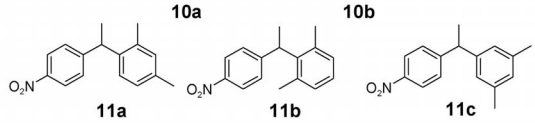
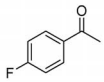
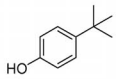
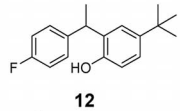
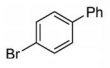
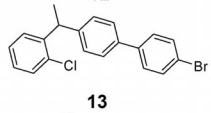
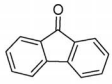
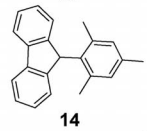
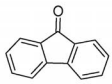
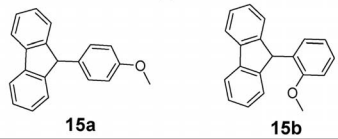


Scheme 3. Reductive arylation reaction of substituted acetophenones and benzaldehydes with aromatic nucleophiles.

In accordance with the general trends of substituent effects in electrophilic aromatic substitution reactions, the formation of *ortho meta* and *para* isomers were observed. However, competition between the first formed 1-chloro-1-phenylethane intermediate and the added arene nucleophile took place. For cases in which the intermediate and nucleophile had similar reactivities, tendency towards dimerization and potential oligomerization of the formed intermediate occurred. This was particularly the case for the reactions of acetophenone with benzene and phenyl bromide, where in the first reaction very little and in the latter case none of the desired coupling product was observed (data not shown). Also, the use of furan or 2-methylfuran as the coupling partner for both acetophenone and benzaldehyde proved inefficient and resulted in the formation of reddish-black gelled solutions with only trace amounts of the desired products detected, possibly a result of coordination of the furan moieties to the iron catalyst, or formation of cross-linked polymers (data not shown). Accordingly, careful selection of the carbonyl compound and the nucleophile reagent applied was necessary for optimization of the reaction yields and regioselectivities. Although the best results and yields were obtained by use of up to a ten-fold excess of arene nucleophile as the solvent, also close to equimolar concentrations of arene reagent were briefly screened with variable results (Table 1, Entries 6, 12 and 13; and Table 2, Entries 7, 9, 14 and 15). As a potential route for preparation of e.g., cyclopentadienyl-type ligand precursors for transition metal complexes, two experiments were carried out with fluorenone as the starting material (Table 1, Entries 14 and 15) providing good yields but only mediocre regioselectivities.

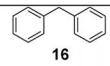
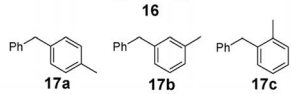
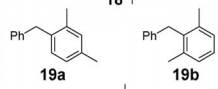
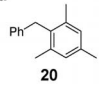
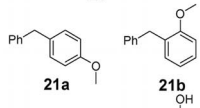
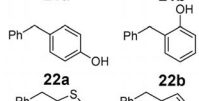
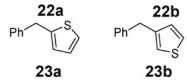
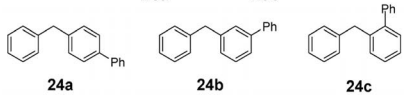
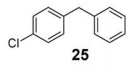
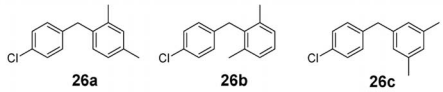
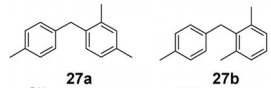
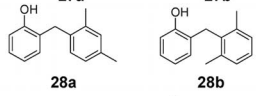
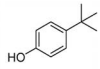
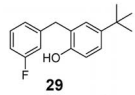
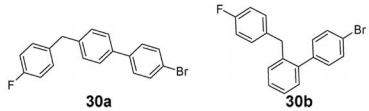
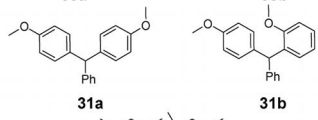
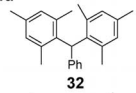
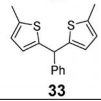
In general, the benzaldehyde derivatives studied proved slightly less reactive than the corresponding acetophenones, which also resulted in poorer regioselectivities in terms of the *ortho*, *meta* and *para* isomers formed. In contrast to the corresponding reaction with acetophenone, the reaction of benzaldehyde with toluene was very slow, resulting in $< 50\%$ isolated yield (Table 1, Entry 1; and Table 2, Entries 1 and 2), whereas the reaction with benzene proceeded without extensive side product formation providing a higher isolated yield. Notably, in accordance with literature precedence,[33] formation of ethers from benzaldehydes was observed. The ethers formed could be converted into the corresponding chlorides by further heating of the reaction mixture with further conversion to form the desired diarylmethane. The compounds prepared in Table 2, Entries 9 and 10,

Table 1. Reductive Friedel–Crafts arylation reaction of acetophenones with substituted arenes (citations refer to characterization data in the literature).[a]

Entry	Electrophile	Nucleophile	Time	Products	Yield[b]	Selectivity[c]
1[17i]			5	 **1a** **1b** **1c**	78	92:1:7
2[28]			3[e]	 **2**	66	–
3[29]			3	 **3a** **3b**	94	100:tr
4[28]			3[e]	 **4**	68	–
5[30]			3	 **5a** **5b**	86	100:tr
6[30]			3[f]	 **6a** **6b**	57	70:30[d]
7[30]			4	 **7a** **7b**	81	81:19
8			3	 **8a** **8b**	69	97:3
9			3	 **9a** **9b**	87	100:tr
10			3	 **10a** **10b**	97	100:tr
11			5	 **11a** **11b** **11c**	87	86:13:1
12			4[f]	 **12**	23	–
13			4[f]	 **13**	76	–
14[31]			7	 **14**	94	–
15[32]			3	 **15a** **15b**	93	64:36[d]

[a] General reaction conditions: Arene reagent used as the solvent unless mentioned otherwise; reaction temperature 50 °C; Et_3SiH was diluted to 1 mL volume with the corresponding arene or dichloromethane solvent and added portionwise at the rate of 0.1 mL/5 min. [b] Isolated yield for the mixture of isomers unless noted otherwise. [c] Determined by GC–MS; tr = trace. [d] Both isomers isolated and characterized separately. [e] Reaction commenced at room temp. [f] Reaction temperature 90 °C. [g] Dichloromethane used as the solvent. [h] Only Me_3SiCl used. [i] Reaction carried out at room temp.

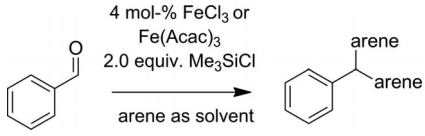
Table 2. Reductive arylation reaction of benzaldehydes with substituted arenes (citations refer to characterization data in the literature).[a]

Entry	Electrophile	Nucleophile	Time	Products	Yield[b]	Selectivity[c]
1[35]			4[f]	 **16**	40	–
2[36]			24[f]	 **17a** **17b** **17c**	48	53:5:42
3[17i]			3[f]	 **18**	78	–
4[17i]			3	 **19a** **19b**	76	82:18
5[37]			3[e, f]	 **20**	80	–
6[37]			6[e]	 **21a** **21b**	81	63:37[d]
7[30]			4[e, g]	 **22a** **22b**	62	52:48[d]
8[38]			6[e]	 **23a** **23b**	50	63:37
9[39]			5[e, g]	 **24a** **24b** **24c**	70	46:1:53
10[40]			4	 **25**	68	–
11			3	 **26a** **26b** **26c**	72	87:13:tr
12			3	 **27a** **27b**	91	87:13
13			2	 **28a** **28b**	39	95:5
14			24[e, g]	 **29**	23	–
15			6[e, g]	 **30a** **30b**	51	56:44[d]
16[41]			5[f, h]	 **31a** **31b**	99	88:12
17[34]			6[f, h]	 **32**	33	–
18[42]			0.5[h, i]	 **33**	96	–

[a] General reaction conditions: Arene reagent used as the solvent unless mentioned otherwise; reaction temperature 50 °C; Et_3SiH was diluted to 1 mL volume with the corresponding arene or dichloromethane solvent and added portionwise at the rate of 0.1 mL/5 min. [b] Isolated yield for the mixture of isomers unless noted otherwise. [c] Determined by GC–MS; tr = trace. [d] Both isomers isolated and characterized separately. [e] Reaction commenced at room temp. [f] Reaction temperature 90 °C. [g] Dichloromethane used as the solvent. [h] Only Me_3SiCl used. [i] Reaction carried out at room temp.

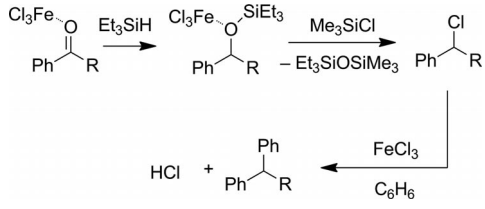
could be considered as potential precursors for Bifonazole and antihistamine synthesis, such as Cetirizine (Figure 1), respectively. Unfortunately, particularly with the compound of Entry 9, in Table 2, where selectivity towards the *para* isomer would be desired for potential use as a pharmaceutical intermediate, significant *para* selectivity was not observed. For these compounds, in an effort to improve the regioselectivity, additional screening experiments were carried out with $FeBr_3$ and FeI_3 (produced in situ from iron and iodine)[27] as the iron catalyst source. The use of $FeBr_3$ as the catalyst increased the reactivity and decreased the reaction time to one third relative to $FeCl_3$, although the reaction still required elevated reaction temperatures to proceed. The regioselectivity was not improved. With FeI_3, neither formation of the desired product nor the reaction intermediate was observed, possibly a result of polymerization of the starting material.

The use of highly electron-rich arenes, such as mesitylene, anisole or thiophene as the nucleophile with benzaldehyde, resulted in the formation of triarylmethanes as side products. Whereas the reaction conditions for Table 2, Entries 5, 6 and 8 were optimized primarily for the corresponding diarylderivatives, it was also of interest to investigate the potential formation of triarylmethanes, similarly to an earlier published method.[34] Here, it was observed that the use of $FeCl_3$ as catalyst, together with at least twofold excess of chlorotrimethylsilane at elevated temperatures, resulted in diarylation of benzaldehyde used (Table 2, Entries 16–18, and Scheme 4). The use of anisole under similar conditions (Table 2, Entry 16) provided a high yield at the expense of regioselectivity. When the same reaction was attempted with thiophene, the use of $FeCl_3$ as catalyst resulted in oligomerization of the diarylated product only as a result of significant increase in reactivity of the substituted thiophene. Also, the use of $FeCl_3$ resulted in some degree of polymerization of the thiophene which made purification tedious. Finally, it was observed that the use of $Fe(acac)_3$ as catalyst instead of $FeCl_3$ suppressed the side reactions, including thiophene polymerization. Consequently, the reaction with 2-methylthiophene was repeated with $Fe(acac)_3$ as catalyst providing the desired triarylmethane (Table 2, Entry 18) in excellent yield. For reaction of benzaldehyde with mesitylene to yield the corresponding triarylmethane (Table 2, Entry 17), various reaction conditions were screened but only poor yields resulted and without complete selectivity towards the desired triaryl compound. Fortunately, the undesired diaryl compound could be separated from the reaction mixture by washing with cold ethanol.



Scheme 4. Reductive arylation reaction of substituted acetophenone and benzaldehyde with aromatic nucleophiles and the corresponding arene as solvent.

Mechanistically the reaction can be suggested to proceed through initial hydrosilylation of the carbonyl group followed by chlorination of the formed silyl ether by the chlorosilane, to yield the corresponding chloride intermediate and siloxane. As postulated earlier by Baba,[26] sufficient oxophilicity and moderate Lewis acidity of the catalyst employed are required for the reaction to proceed. In the first exothermic reaction step, siloxane formation functions as the driving force for formation of the chloride. It is unclear at present if the chlorination reaction is fully iron catalyzed or the formation of a $Me_3SiCl–FeCl_3$ type complex, similar to $Me_3SiCl–InCl_3$ complex formation observed earlier by Baba et al.,[22a,22b] influences the first reaction steps. Such influence appears reasonable, considering that the addition of chloromethylsilane to the reaction mixture facilitates the dissolution of the $FeCl_3$ catalyst. In the absence of chloromethylsilane, the reaction slowly proceeds as a Clemmens-type reduction. The tentative reaction mechanism from chlorination to Friedel–Crafts alkylation is illustrated in Scheme 5. The possible influence of chlorotrimethylsilane and the siloxane formed in the Friedel–Crafts alkylation of benzyl chloride with benzene was briefly investigated experimentally. Although the addition of chlorotrimethylsilane helps to keep the $FeCl_3$ catalyst dissolved, it does not significantly influence the actual alkylation reaction. Addition of one equivalent of hexamethylsiloxane, in turn, does not influence the dissolution of $FeCl_3$ but slows down the reaction rate at lower temperatures, possibly owing to coordination of the siloxane to the iron catalyst, rendering it less active for the desired Friedel–Crafts alkylation reaction. Finally, a brief investigation of potential secondary kinetic isotope effects was conducted with 2′,3′,4′,5′,6′-d_5-acetophenone, 2,2,2-d_3-acetophenone, as well as acetophenone in combination with triethyl(silane-*d*) without detectable influence on the rate of the reaction.



Scheme 5. Tentative mechanism for the iron-catalyzed Friedel–Crafts alkylation.

Conclusions

To summarize, a simple and efficient iron-catalyzed method for arylation of aromatic carbonyl compounds has been developed by using 4 mol-% $FeCl_3$ or $Fe(acac)_3$ as the catalyst in combination with excess chlorotrimethylsilane and triethylsilane. In the reactions studied here, the desired coupling products were obtained in 23–97% yields with regioselectivities ranging from poor to moderate, being similar to the yields and selectivities obtained earlier[19–23] in studies that used benzylic carbonyl compounds as the benz-

ylating agents. The developed method was successfully applied to a wide range of aromatic ketones and aldehydes and resulted in the isolation of several previously undisclosed compounds (Table 1, Entries 8–13 and Table 2, Entries 10–15) potentially useful as precursors for further derivatization. Notably, previous studies that used benzylic carbonyl compounds as starting materials generally reported only NMR and/or GC yields for the products, whereas in the present work isolated yields for accurately characterized compounds are given. In contrast to other catalytic benzylation reactions that use benzylic alcohols or acetylated derivatives, the present method provides similar efficiencies, with some variations depending on the reactants used. Benzylic chloride starting materials often have limited commercial availability, whereas several benzaldehyde and acetophenone derivatives are readily available. The products prepared here would also be accessible through a multistep reaction route involving carbonyl reduction and chlorination of the alcohol formed, followed by subsequent Friedel–Crafts alkylation, requiring typically several days to perform. The presently described direct iron-catalyzed method is robust and allows for the rapid preparation of diphenylmethane and ethane derivatives, as well as selected triphenylmethane and fluorene derivatives. Although this new methodology is limited by the general constrains that arise from Friedel–Crafts alkylation and the use of chlorosilane, it can be efficiently applied in selected applications, including the potential production of complex molecules and intermediates for pharmaceuticals. In future work, we aim to expand the methodology towards non-benzylic aldehydes and ketones. Studies to provide a deeper understanding for the mechanism of the chlorination reaction are also planned.

Experimental Section

General Considerations: All chemicals were purchased from commercial sources and were used without further purification unless mentioned otherwise. The NMR spectra were recorded with a 600 MHz or 500 MHz NMR spectrometer. The 600 MHz instrument was equipped with a BBI-5 mm-Zgrad-ATM probe or BBO-5 mm-Zgrad probe at 298 K operating at 600.13 MHz for ^{1}H and 150.92 MHz for ^{13}C. The 500 MHz instrument was equipped with a BBI-5 mm-Zgrad-ATM probe or BBO-5 mm-Zgrad probe at 298 K operating at 500.13 MHz for ^{1}H and 125.76 MHz for ^{13}C. The chemical shifts were calibrated to the residual proton and carbon resonance of the solvent. Product distributions and purities were monitored by GC–MS. The GC–MS instrument was equipped with an MS detector (EI), HP-5MS column (30 m × 250 μm × 0.25 μm), and He was used as the carrier gas with the following temperature program: injector 250 °C, oven $T_{initial}$ = 50 °C (4 min), rate 10 °C/min, T_{final} = 300 °C, hold 5 min. The purity of the products is at least 99% unless indicated otherwise. The HRMS were recorded with Q-TOF with electrospray ionization operated in negative mode. IR spectra were recorded with FT-IR with Platinum single reflection diamond ATR module. Elemental analysis was performed with FLASH 2000, which resulted, unfortunately, in poor reproducibility for some compounds, particularly for **11**, **26** and **27** for which accurate data could not be obtained. The results reported for these compounds are, therefore, provided only to illustrate the best values obtained. The NMR and MS data are consistent with high purity in each case. Column chromatography was performed on Redi*Sep* R_f Gold Silica columns (0.020–0.040 mm).

General Procedure for Reaction Work-Up: After cooling to room temperature, the reaction mixture was diluted with EtOAc (10 mL) and washed twice with saturated sodium hydrogen carbonate solution (3 mL). The aqueous phases were combined and washed with EtOAc (3 mL). The organic fractions were combined, dried with sodium sulfate, evaporated and purified by flash chromatography.

General Method A: Into the corresponding arene (1 mL) was suspended $FeCl_3$ (11 mg, 0.07 mmol), followed by addition of the aryl ketone or aryl aldehyde (1.76 mmol), respectively. Next, chlorotrimethylsilane (0.25 mL, 1.94 mmol) was added to the reaction mixture, which dissolved the $FeCl_3$. Then, triethylsilane (0.30 mL, 1.85 mmol) was diluted with the corresponding arene (total volume of 1 mL) and added portionwise (0.1 mL/every 5 min). The resulting solution was stirred for a total of 2 h at room temperature and then heated to 50 °C (or to 90 °C) and stirred until full conversion followed by general work up.

General Method B: Into the corresponding arene (1 mL) was suspended $FeCl_3$ (11 mg, 0.07 mmol), followed by addition of the aryl aldehyde (1.76 mmol). Next, chlorotrimethylsilane (0.25 mL, 1.94 mmol) was added to the reaction mixture, which dissolved the $FeCl_3$, followed by heating to 50 °C (or to 90 °C). Then, triethylsilane (0.30 mL, 1.85 mmol) was diluted with the corresponding arene (total volume of 1 mL) and added portionwise (0.1 mL/every 5 min) to the reaction mixture, which then was stirred until full conversion followed by general work up.

General Method C: Into the corresponding solvent (1 mL of arene or 0.3 mL of dichloromethane) was suspended $FeCl_3$ (11 mg, 0.07 mmol), followed by addition of the aryl ketone or aryl aldehyde (1.76 mmol). Next, chlorotrimethylsilane (0.25 mL, 1.94 mmol) was added to the reaction mixture, which dissolved the $FeCl_3$, followed by addition of triethylsilane (0.30 mL, 1.85 mmol), which was diluted with the respective arene/solvent (total volume of 1 mL) and added portionwise (0.1 mL/every 5 min). Afterwards the nucleophile was added (in case of dichloromethane) and stirred at elevated temperature until full conversion followed by general work up.

1-Methyl-4-(1-phenylethyl)benzene (1): Method A with toluene at 50 °C. Total reaction time 5 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 78% (268 mg), ratio of isomers *p*:*m*:*o* (**1a/1b/1c**) 92:1:7. R_f = 0.66 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[17i]

1,4-Dimethyl-2-(1-phenylethyl)benzene (2): Method A with *para*-xylene at 90 °C. Total reaction time 3 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 66% (246 mg). R_f = 0.66 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[28]

2,4-Dimethyl-1-(1-phenylethyl)benzene (3): Method A with *meta*-xylene at 50 °C. Total reaction time 3 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 94% (347 mg), ratio of isomers *p*:*o* (**3a/3b**) 100:trace, R_f = 0.66 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[29]

1,3,5-Trimethyl-2-(1-phenylethyl)benzene (4): Method A with mesitylene at 90 °C. Total reaction time 3 h, after which the washed

crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 68% (268 mg). Purity: 97%. R_f = 0.57 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[28]

1-Methoxy-4-(1-phenylethyl)benzene (5): Method A with anisole at 50 °C. Total reaction time 3 h, after which the washed crude product was purified with flash chromatography (0–25% dichloromethane/hexane) to yield a colorless oil, yield 86% (321 mg), ratio of isomers *p*:*o* (**5a/5b**) 100:trace. Purity: 97%. R_f = 0.20 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[30]

4-(1-Phenylethyl)phenol (6): Method C with dichloromethane as solvent. After 2 h at room temperature, phenol (0.50 g, 5.28 mmol) was added. The reaction mixture was stirred at 50 °C for 3 h. Crude product was purified by flash chromatography (0–15%, EtOAc/hex) to yield both isomers separately as colorless oils, yield *para* isomer **6a**: 40% (140 mg), Purity: 97%. R_f = 0.52 (1:3 EtOAc/hexane); *ortho* isomer **6b**: 17% (59 mg), R_f = 0.62 (1:3 EtOAc/hexane). Characterization data is consistent with that published previously.[30]

2-(1-Phenylethyl)thiophene (7): Method A with thiophene at 50 °C. Total reaction time 4 h, after which the washed crude product was purified by flash chromatography with hexane to yield a slightly yellow oil, yield 81% (268 mg), ratio of isomers 2:3 (**7a/7b**) 81:19. R_f = 0.52 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[30]

2,4-Dimethyl-1-[1-(4-methylphenyl)ethyl]benzene (8): Method A with *meta*-xylene at 50 °C. Total reaction time 3 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 69% (272 mg), ratio of isomers *p*:*o* (**8a/8b**) 97:3. R_f = 0.76 (dichloromethane/hexane, 1:3). ^{1}H NMR (CD_2Cl_2, 500.13 MHz, 25 °C): δ = 7.16 (d, J = 8.1 Hz, 1 H), 7.11–7.06 (m, 4 H), 7.03 (br. d, J = 7.9 Hz, 1 H), 6.98 (br. s, 1 H), 4.28 (q, J = 7.2 Hz, 1 H), 2.32 (s, 3 H), 2.31 (s, 3 H), 2.23 (s, 3 H), 1.58 (d, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (CD_2Cl_2, 125.76 MHz, 25 °C): δ = 143.5, 141.7, 136.2, 135.8, 135.7, 131.5, 129.3, 127.9, 127.0, 126.8, 40.6, 22.4, 21.1, 21.0, 19.9 ppm. IR (film): $\tilde{\nu}_{max}$ = 2965, 1511, 1450, 1371, 1044 cm^{-1}. MS (EI): m/z = 224 [M$^+$]. $C_{17}H_{20}$ (224.35): calcd. C 91.0, H 9.0; found C 90.9, H 8.9.

1-[1-(4-Bromophenyl)ethyl]-2,4-dimethylbenzene (9): Method A with *meta*-xylene at 50 °C. Total reaction time 3 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 87% (445 mg), ratio of isomers *p*:*o* (**9a/9b**) 100:trace. R_f = 0.80 (dichloromethane/hexane, 1:3). ^{1}H NMR (CD_2Cl_2, 600.13 MHz, 25 °C): δ = 7.80 (td, J = 2.3, 8.9 Hz, 2 H), 7.11 (d, J = 7.8 Hz, 1 H), 7.04 (td, J = 2.3, 8.9 Hz, 2 H), 7.01 (br. d, J = 7.8 Hz, 1 H), 6.96 (s, 1 H), 4.25 (q, J = 7.2 Hz, 1 H), 2.28 (s, 3 H), 2.18 (s, 3 H), 1.55 (d, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (CD_2Cl_2, 150.92 MHz, 25 °C): δ = 146.2, 140.8, 136.19, 136.15, 131.63, 131.61, 129.9, 127.1, 126.8, 119.7, 40.5, 22.2, 21.0, 19.7 ppm. IR (film): $\tilde{\nu}_{max}$ = 2966, 1485, 1450, 1102, 1008 cm^{-1}. MS (EI): m/z = 288/290 [M$^+$]. $C_{16}H_{17}Br$ (289.21): calcd. C 66.5, H 5.9; found C 66.4, H 5.9.

1-[1-(2-Chlorophenyl)ethyl]-2,4-dimethylbenzene (10): Method A with *meta*-xylene at 50 °C. Total reaction time 3 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 97% (419 mg), ratio of isomers *p*:*o* (**10a/10b**) 100:trace. R_f = 0.73 (dichloromethane/hexane, 1:3). ^{1}H NMR (CD_2Cl_2, 500.13 MHz, 25 °C): δ = 7.36 (dd, J = 1.6, 7.7 Hz, 1 H), 7.20–7.13 (m, 2 H), 7.11–7.07 (m, 2 H), 7.00 (br. d, J = 7.9 Hz, 1 H), 6.98 (br. s, 1 H), 4.65 (q, J = 7.3 Hz, 1 H), 2.30 (s, 3 H), 2.18 (s, 3 H), 1.54 (d, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (CD_2Cl_2, 125.76 MHz, 25 °C): δ = 144.3, 140.4, 136.6, 136.1, 134.1, 131.5, 129.8, 128.9, 127.6, 127.3, 126.9, 126.7, 37.9, 21.0, 20.8, 19.4 ppm. IR (film): $\tilde{\nu}_{max}$ = 2968, 1470, 1439, 1034 cm^{-1}. MS (EI): m/z = 244 [M$^+$]. $C_{16}H_{17}Cl$ (244.76): calcd. C 78.5, H 7.00; found C 78.6, H 6.9.

1,5-Dimethyl-2-[1-(4-nitrophenyl)ethyl]benzene (11): Method A with *meta*-xylene at 50 °C. Total reaction time 5 h, after which the washed crude product was purified with flash chromatography (0–30% dichloromethane/hexane) to yield a pale yellow oil, which slowly solidified, yield 87% (398 mg), ratio of isomers *p*:*o*:*m* (**11a/11b/11c**) 86:13:1. R_f = 0.31 (dichloromethane/hexane, 1:3). For major isomer: ^{1}H NMR (CD_2Cl_2, 600.13 MHz, 25 °C): δ = 8.09 (td, J = 2.2, 9.2 Hz, 2 H), 7.32 (td, J = 2.2, 9.2 Hz, 2 H), 7.13 (d, J = 7.9 Hz, 1 H), 7.03 (br. d, J = 7.9 Hz, 1 H), 6.98 (s, 1 H), 4.39 (q, J = 7.5 Hz, 1 H), 2.29 (s, 3 H), 2.17 (s, 3 H), 1.61 (d, J = 7.5 Hz) ppm. ^{13}C NMR (CD_2Cl_2, 150.92 MHz, 25 °C): δ = 155.0, 146.6, 139.8, 136.6, 136.3, 131.8, 128.9, 127.3, 126.9, 123.9, 41.2, 22.0, 21.0, 19.8 ppm. $\tilde{\nu}_{max}$ (solid) = 3074, 2964, 1592, 1342, 1110 cm^{-1}. MS (EI): m/z = 255 [M$^+$]. $C_{16}H_{17}NO_2$ (255.32): calcd. C 75.3, N 5.5, H 6.7; found C 74.6, N 5.5, H 6.7. Inconsistency in the carbon analysis is possibly a result of volatility issues in the mass analysis (see also General Considerations).

2-[1-(4-Fluorophenyl)ethyl]-4-(1,1-dimethylethyl)phenol (12): Method C with dichloromethane as solvent and 4-fluoroacetophenone (0.21 mL, 1.76 mmol). After 2 h at room temperature, 4-*tert*-butylphenol (0.30 g, 2.02 mmol) was added. The reaction mixture was heated to 50 °C and stirred for 2 h. Crude product was purified by flash chromatography (0–15% EtOAc/hexane) to yield a slightly yellow oil, yield 35% (170 mg) Purity = 98%. R_f = 0.49 (1:4 EtOAc/hex). ^{1}H NMR (CD_2Cl_2, 600.13 MHz, 25 °C): δ = 7.25 (d, J = 2.5 Hz, 1 H), 7.24–7.20 (m, 2 H), 7.13 (dd, J = 2.5, 8.4 Hz, 1 H), 6.98 (tt, J = 2.5, 9.1 Hz, 2 H), 6.66 (d, J = 8.4 Hz, 1 H), 4.60 (b, 1 H), 4.39 (q, J = 7.2 Hz, 1 H), 1.61 (d, J = 7.2 Hz, 3 H), 1.29 (s, 9 H) ppm. ^{13}C NMR (CD_2Cl_2, 150.92 MHz, 25 °C): δ = 161.6 (d, $J_{C,F}$ = 243 Hz), 151.2, 144.0, 142.2 (d, $J_{C,F}$ = 4 Hz), 131.5, 129.4 (d, $J_{C,F}$ = 8 Hz), 125.2, 124.6, 115.5 (d, $J_{C,F}$ = 5 Hz), 115.3, 38.5, 34.5, 31.7, 21.2 ppm. IR (film): $\tilde{\nu}_{max}$ = 3287, 2964, 1600, 1505, 1219, 1125 cm^{-1}. MS (EI): m/z = 272 [M$^+$]. HRMS (ESI): calcd. for $C_{18}H_{21}FO$ (M – H) 271.1504; found 271.1509.

4-Bromo-4′-[1-(2-chlorophenyl)ethyl]-1,1′-biphenyl (13): Method C with dichloromethane as solvent and 2′-chloroacetophenone (0.23 mL, 1.76 mmol). After 2 h at room temperature, 4-bromobiphenyl (0.47 g, 2.02 mmol) was added. The reaction mixture was heated to 50 °C and stirred for 2 h. Crude product was purified by flash chromatography (hexane) to yield a colorless oil, which slowly solidified, yield 76% (499 mg). R_f = 0.60 (dichloromethane/hexane, 1:3). ^{1}H NMR (CD_2Cl_2, 600.13 MHz, 25 °C): δ = 7.55 (td, J = 2.3, 9.0 Hz, 2 H), 7.50 (td, J = 2.1, 8.7 Hz, 2 H), 7.46 (td, J = 2.3, 9.0 Hz, 2 H), 7.37 (dd, J = 1.6, 7.9 Hz, 1 H), 7.33–7.29 (m, 3 H), 7.27 (dt, J = 1.3, 7.6 Hz, 1 H), 7.18 (dt, J = 1.6, 7.6 Hz, 1 H), 4.68 (q, J = 7.3 Hz, 1 H), 1.64 (d, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (CD_2Cl_2, 150.92 MHz, 25 °C): δ = 145.2, 143.7, 140.2, 138.1, 134.2, 132.2, 130.0, 129.0, 128.9, 128.7, 127.9, 127.4, 127.2, 121.6, 41.1, 21.4 ppm. $\tilde{\nu}_{max}$ (solid) = 3059, 2970, 1472, 1388, 1058 cm^{-1}. MS (EI): m/z = 370/372 [M$^+$]. $C_{20}H_{16}BrCl$ (371.70): calcd. C 64.6, H 4.3; found C 64.6, H 4.3.

9-(2,4,6-Trimethylphenyl)-9*H*-fluorene (14): Method A with mesitylene at 50 °C. Total reaction time 7 h, after which the washed crude product was purified by flash chromatography with hexane to yield a colorless oil, yield 94% (472 mg), R_f = 0.47 (dichloro-

methane/hexane, 1:3). Characterization data is consistent with that published previously.[31]

9-(4-Methoxyphenyl)-9*H*-fluorene (15): Method A with anisol at 50 °C. Total reaction time 3 h, after which the washed crude product was purified by flash chromatography (0–40% dichloromethane/hexane) to yield both isomers as white solids, yield *para* isomer **15a**: 61% (293 mg). R_f = 0.14 (dichloromethane/hexane, 1:3). *ortho* isomer **15b**: 35% (166 mg). R_f = 0.29 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[32]

Diphenylmethane (16): Method B with benzene at 90 °C and 32 mg (0.14 mmol) of $FeCl_3$. Total reaction time 4 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 40% (117 mg). R_f = 0.65 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[35]

1-Methyl-4-(phenylmethyl)benzene (17): Method B with toluene at 90 °C. Total reaction time 24 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 48% (155 mg), ratio of isomers *p*:*m*:*o* (**17a/17b/17c**) 53:5:42. R_f = 0.73 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[36]

1,4-Dimethyl-2-(phenylmethyl)benzene (18): Method B with *para*-xylene at 90 °C. Total reaction time 3 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 78% (269 mg). R_f = 0.73 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[17i]

2,4-Dimethyl-1-(phenylmethyl)benzene (19): Method B with *meta*-xylene at 50 °C. Total reaction time 3 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 76% (264 mg), ratio of isomers *p*:*o* (**19a/19b**) 82:18. R_f = 0.67 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[17i]

1,3,5-Trimethyl-2-[(4-methylphenyl)methyl]benzene (20): Method C with mesitylene as solvent. Total reaction time 3 h at room temp. and 2 h at 90 °C, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 80% (297 mg). R_f = 0.70 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[37]

1-Methoxy-4-(phenylmethyl)benzene (21): Method C with dichloromethane as solvent. After 2 h at room temperature, anisole (1.5 mL, 13.8 mmol) was added. The reaction mixture was then heated to 50 °C and stirred for 4 h. The crude product was purified by flash chromatography (0–40% dichloromethane/hexane) to yield both isomers separately as colorless oils, yield *para* isomer **21a**: 51% (178 mg), ratio of isomers *p*:*o* (**21a/21b**) 99:1, Purity = 95%. R_f = 0.32 (dichloromethane/hexane, 1:3). *ortho* isomer **21b**: 30% (103 mg). R_f = 0.43. Characterization data is consistent with that published previously.[37]

4-(Phenylmethyl)phenol (22): Method C with dichloromethane as solvent. After 2 h at room temperature, phenol (0.50 g, 5.28 mmol) was added. The reaction mixture was then heated to 50 °C and additional $FeCl_3$ (11 mg, 0.07 mmol) was added after 1 h. The mixture was stirred for additional 1 h. Crude product was purified by flash chromatography (0–15% EtOAc/hexane) to yield both isomers separately as yellowish oils from which the *para* isomer **22a** slowly crystallized, yield *para* isomer **22a**: yield 32% (104 mg). Purity: 97%. R_f = 0.43 (1:4 EtOAc/hexane); *ortho* isomer **22b**: 30% (96 mg), purity: 95%. R_f = 0.57 (1:4 EtOAc/hexane). Characterization data is consistent with that published previously.[30]

2-(Phenylmethyl)thiophene (23): Method C with dichloromethane as solvent. After 2 h at room temperature, thiophene (1.5 mL, 18.7 mmol) was added. The reaction mixture was then heated to 50 °C and stirred for 4 h. Crude product was purified by flash chromatography with hexane to yield a colorless oil, yield 50% (157 mg), ratio of isomers 2:3 (**23a/23b**); 63:37. R_f = 0.62 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[38]

4-(Phenylmethyl)-1,1′-biphenyl (24): Method C with dichloromethane as solvent. After 2 h at room temperature, biphenyl (0.55 g, 3.56 mmol) was added. The reaction mixture was heated to 50 °C and stirred for 3 h. The crude product was purified twice by flash chromatography (hexane) to yield *ortho* isomer **24c** as a colorless oil and *para* isomer **24a** as a white solid. *para* Isomer **24a**: yield 36% (155 mg) *p*:*m*:*o* (**24a/24b/24c**) 97:2:1. R_f = 0.44 (dichloromethane/hexane, 1:3). *ortho* Isomer **24b**: yield 34% (147 mg). R_f = 0.51 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[39]

1-Chloro-4-(phenylmethyl)benzene (25): Method B with benzene at 50 °C. Total reaction time: 4 h, after which the washed crude product was purified by flash chromatography (hexane) to yield a colorless oil, yield 68% (243 mg). R_f = 0.58 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[40]

1-[(4-Chlorophenyl)methyl]-2,4-dimethylbenzene (26): Method B with *meta*-xylene at 50 °C. Total reaction time 3 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 72% (309 mg), ratio of isomers *o*:*m*:*p p*:*o*:*m* (**26a/26b/26c**) 87:13:trace. R_f = 0.80 (dichloromethane/hexane, 1:3). For the mixture of isomers: ^{1}H NMR (CD_2Cl_2, 500.13 MHz, 25 °C): δ = 7.27–7.22 (m, 2 H, **26a** + 2 H, **26b**), 7.12–7.07 (m, 2 H, **26a** + 3 H, **26b**), 7.02–6.97 (m, 3 H, **26a** + 2 H, **26b**), 4.05 (s, 2 H, **26b**), 3.93 (s, 2 H, **26a**), 2.32 (s, 3 H, **26a**), 2.25 (s, 6 H, **26b**), 2.20 (s 3 H, **26a**) ppm. ^{13}C NMR (CD_2Cl_2, 125.76 MHz, 25 °C): δ = 140.0, 139.1, 137.5, 136.9, 136.8, 136.6, 135.9, 131.8, 131.6, 130.5, 130.2, 129.7, 128.8, 128.6, 127.1, 126.9, 38.7, 34.7, 21.1, 20.3, 19.7 ppm. IR (film): $\tilde{\nu}_{max}$ = 2918, 1488, 1442, 1091, 1033 cm^{-1}. MS (EI): *m*/*z* = 230 [M$^+$]. $C_{15}H_{15}Cl$ (230.74): calcd. C 78.1, H 6.6; found C 77.5, H 6.4. Inconsistency in the carbon analysis is possibly a result of volatility issues in the mass analysis (see also General Considerations).

2,4-Dimethyl-1-[(4-methylphenyl)methyl]benzene (27): Method B with *meta*-xylene at 50 °C. Total reaction time 3 h, after which the washed crude product was purified with flash chromatography with hexane to yield a colorless oil, yield 91% (337 mg), ratio of isomers *p*:*o* (**27a/27b**) 87:13. R_f = 0.76 (dichloromethane/hexane, 1:3). For the mixture of isomers: ^{1}H NMR (CD_2Cl_2, 500.13 MHz, 25 °C): δ = 7.12–7.01 (m, 6 H, **27a** + 5 H, **27b**), 6.99–6.93 (m, 1 H, **27a** + 2 H, **27b**), 4.04 (s, 2 H, **27b**), 3.93 (s, 2 H, **27a**), 2.33 (s, 3 H, **27a**), 2.32 (s, 3 H, **27a**, 3 H, **27b**), 2.27 (s, 6 H, **27b**), 2.23 (s, 3 H, **27a**) ppm. ^{13}C NMR (CD_2Cl_2, 125.76 MHz, 25 °C): δ = 138.2, 137.7, 137.5, 137.2, 136.73, 136.70, 136.2, 135.8, 135.6, 131.4, 130.1, 129.4, 128.9, 128.4, 128.1, 126.9, 126.6, 38.9, 34.9, 21.10, 21.06, 20.4, 19.8 ppm. IR (film): $\tilde{\nu}_{max}$ = 2918, 1512, 1442, 1116, 1034, 1021 cm^{-1}. MS (EI): *m*/*z* = 210 [M$^+$]. $C_{16}H_{18}$ (210.32): calcd. C 91.4, H 8.6; found C 88.4, H 8.4. Inconsistency in the carbon analysis is possibly a result of volatility issues in the mass analysis (See also General Considerations).

2-[(2,4-Dimethylphenyl)methyl]phenol (28): Method B with *meta*-xylene at 50 °C. Total reaction time 2 h, after which the washed

crude product was purified with flash chromatography (0–15% EtOAc/hexane) to yield a colorless oil, yield 39% (144 mg), ratio of isomers *o*:*m*:*p* 5:0:95. R_f = 0.50 (1:4 EtOAc/hexane). For major isomer: ^{1}H NMR (CD_2Cl_2, 600.13 MHz, 25 °C): δ = 7.11 (dt, J = 1.4, 7.8 Hz, 1 H), 7.02 (s 1 H), 6.96–6.92 (m, 3 H), 6.85 (dt, J = 1.4, 7.8 Hz, 1 H), 6.79 (dd, J = 0.9, 8.2 Hz, 1 H), 4.85 (b, 1 H), 3.92 (s, 2 H), 2.30 (s, 3 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (CD_2Cl_2, 150.92 MHz, 25 °C): δ = 154.2, 137.0, 136.5, 135.1, 131.5, 130.9, 129.4, 127.9, 127.1, 127.0, 121.2, 115.8, 33.5, 21.0, 19.7 ppm. IR (film): $\tilde{\nu}_{max}$ = 3520, 2917, 1589, 1499, 1452, 1205, 1069 cm^{-1}. MS (EI): *m*/*z* = 212 [M$^+$]. HRMS (ESI): calcd. for $C_{15}H_{16}O$ (M – H) 211.1128; found 211.1119.

2-[1-(3-Fluorophenyl)methyl]-4-(1,1-dimethylethyl)phenol (29): Method C with dichloromethane as solvent and 3-fluorobenzaldehyde (0.19 mL, 1.76 mmol). After 2 h at room temperature, 4-*tert*-butylphenol (0.30 g, 2.02 mmol) was added. The reaction mixture was then heated to 50 °C and stirred for 22 h. Crude product was purified with flash chromatography (0–15% EtOAc/hexane) to yield a slightly yellow oil, yield 23% (103 mg). R_f = 0.46 (1:4 EtOAc/hexane). ^{1}H NMR (CD_2Cl_2, 600.13 MHz, 25 °C): δ = 7.25 (td, J = 6.2, 8.0 Hz, 1 H), 7.17–7.14 (m, 2 H), 7.04 (d, J = 8.0 Hz, 1 H), 6.93 (br. d, J = 10.2 Hz, 1 H), 6.89 (dt, J = 2.5, 8.4 Hz, 1 H), 6.71 (d, J = 8.4 Hz, 1 H), 4.68 (b, 1 H), 3.97 (s, 2 H), 1.28 (s, 9 H) ppm. ^{13}C NMR (CD_2Cl_2, 150.92 MHz, 25 °C): δ = 163.4 (d, $J_{C,F}$ = 244 Hz), 151.7, 144.3, 144.0 (d, $J_{C,F}$ = 7 Hz), 130.2 (d, $J_{C,F}$ = 10 Hz), 128.4, 125.2, 124.7 (d, $J_{C,F}$ = 2 Hz), 115.7 (d, $J_{C,F}$ = 21 Hz), 115.4, 113.2 (d, $J_{C,F}$ = 20 Hz), 36.6 (d, $J_{C,F}$ = 2 Hz), 34.3, 31.7 ppm. IR (film): $\tilde{\nu}_{max}$ = 3288, 2956, 1615, 1589, 1504, 1234, 1180 cm^{-1}. MS (EI): *m*/*z* = 258 [M$^+$]. HRMS (ESI): calcd. for $C_{17}H_{19}FO$ (M – H) 257.1347; found 257.1335.

4-Bromo-4′-[(4-fluorophenyl)methyl]-1,1′-biphenyl (30): Method C with dichloromethane as solvent and 4-fluorobenzaldehyde (0.19 mL, 1.76 mmol). After 2 h at room temperature, 4-bromobiphenyl (0.47 g, 2.02 mmol) was added. Temperature was raised to 50 °C and stirred for 4 h. Crude product was purified by flash chromatography (hexane) to yield both isomers separately with the *ortho* isomer as colorless oil which slowly solidified and the *para* isomer as a white solid. *para* Isomer **30a**: yield 29% (172 mg). R_f = 0.43 (dichloromethane/hexane, 1:3). *ortho* Isomer **30b**: yield 22% (135 mg). R_f = 0.50 (dichloromethane/hexane, 1:3). *para* Isomer **30a**: ^{1}H NMR (CD_2Cl_2, 600.13 MHz, 25 °C): δ = 7.56 (td, J = 2.3, 8.8 Hz, 2 H), 7.50 (td, J = 2.0, 8.3 Hz, 2 H), 7.46 (td, J = 2.4, 8.9 Hz, 2 H), 7.26 (d, J = 8.4 Hz, 2 H), 7.22–7.18 (m, 2 H), 7.00 (tt, J = 2.4, 8.9 Hz, 2 H), 3.99 (s, 2 H) ppm. ^{13}C NMR (DMSO, 150.92 MHz, 25 °C): δ = 161.9 (d, $J_{C,F}$ = 243 Hz), 141.2, 140.2, 138.2, 137.3 (d, $J_{C,F}$ = 3 Hz), 132.2, 130.7 (d, $J_{C,F}$ = 8 Hz), 129.7, 129.0, 121.6, 115.6 (d, $J_{C,F}$ = 21 Hz), 41.0 ppm. $\tilde{\nu}_{max}$ (solid) = 2903, 1601, 1508, 1476, 1238 cm^{-1}. MS (EI): *m*/*z* = 340/342 [M$^+$]. $C_{19}H_{14}BrF$ (341.22): calcd. C 66.9, H 4.1; found C 66.9, H 4.1. *ortho* Isomer **30b**: ^{1}H NMR (CD_2Cl_2, 600.13 MHz, 25 °C): δ = 7.50 (td, J = 2.3, 8.9 Hz, 2 H), 7.34–7.27 (m, 3 H), 7.24–7.20 (m, 2 H), 7.10 (td, J = 2.3, 8.9 Hz, 2 H), 7.89 (br. d, J = 7.4 Hz, 4 H), 3.91 (s, 2 H) ppm. ^{13}C NMR (CD_2Cl_2, 150.92 MHz, 25 °C): δ = 161.6 (d, $J_{C,F}$ = 243 Hz), 141.4, 141.0, 138.5, 137.5 (d, $J_{C,F}$ = 4 Hz), 131.5, 131.4, 130.7, 130.5, 130.4 (d, $J_{C,F}$ = 4 Hz), 128.3, 126.9, 121.4, 115.3, (d, $J_{C,F}$ = 21 Hz), 38.6 ppm. IR (film): $\tilde{\nu}_{max}$ = 3045, 1605, 1508, 1474, 1222 cm^{-1}. MS (EI): *m*/*z* = 340/342 [M$^+$]. $C_{19}H_{14}BrF$ (341.22): calcd. C 66.9, H 4.1; found C 66.8, H 4.1.

4,4′-Dimethoxytrityl (31): Into anisole (1.7 mL) was suspended $FeCl_3$ (11 mg, 0.07 mmol) and benzaldehyde (0.18 mL, 1.76 mmol) was added. Next, chlorotrimethylsilane (0.25 mL, 1.94 mmol) was added to the reaction mixture, which dissolved the $FeCl_3$. The mixture was heated to 90 °C and stirred for 5 h followed by general work up and purification by flash chromatography (0–40% dichloromethane/hexane) to yield a colorless liquid, which slowly solidified, yield 99% (531 mg), ratio of isomers pp:op (**31a/31b**) 88:12. R_f = 0.21 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[41]

1,1′-(Phenylmethylene)bis[2,4,6-trimethylbenzene] (32): Into mesitylene (1.7 mL) was suspended $FeCl_3$ (11 mg, 0.07 mmol) and benzaldehyde (0.18 mL, 1.76 mmol) was then added. Next, chlorotrimethylsilane (0.45 mL, 3.52 mmol) was added to the reaction mixture, which dissolved the $FeCl_3$. The mixture was heated to 90 °C and stirred for 6 h, followed by general work up and purification by flash chromatography with hexane to yield a colorless oil, which, when dissolved in ethanol, instantly solidified to a white powder. The mixture was kept at 4 °C overnight, the powder formed was separated and dried in vacuo, yield 33% (190 mg). R_f = 0.58 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[34]

2,2′-(Phenylmethylene)bis[5-methylthiophene] (33): Into 2-methylthiophene (1.7 mL), was suspended $Fe(acac)_3$ (12 mg, 0.035 mmol) and after benzaldehyde (0.18 mL, 1.76 mmol) was added. Next, chlorotrimethylsilane (0.25 mL, 1.94 mmol) was added to the mixture dissolving the $FeCl_3$, reaction was stirred at room temp. for 30 min followed by general work up and purification by flash chromatography (hexane) to yield a colorless liquid, which slowly solidified in the freezer to form a white solid, yield 92% (460 mg), R_f = 0.53 (dichloromethane/hexane, 1:3). Characterization data is consistent with that published previously.[42]

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H NMR and ^{13}C NMR spectra and GC–MS chromatograms of all final products.

Acknowledgments

Financial support to R. S. from the National Doctoral Program of Organic Chemistry and Chemical Biology (2010–2013), Stiftelsen för Åbo Akademi, Orion Farmos Research Foundation and Magnus Ehrnrooth Foundation is gratefully acknowledged.

[1] For reviews, see: a) C. Bolm, J. Legros, J. L. Paith, L. Zani, *Chem. Rev.* **2004**, *104*, 6217–6254; b) A. Correa, O. G. Mancheño, C. Bolm, *Chem. Soc. Rev.* **2008**, *37*, 1108–1117; c) E. B. Bauer, *Curr. Org. Chem.* **2008**, *12*, 1341–1369; d) X. Sun, J. Li, X. Huang, C. Sun, *Curr. Inorg. Chem.* **2012**, *2*, 64–85; e) C.-L. Sun, B.-J. Li, Z.-J. Sun, *Chem. Rev.* **2011**, *111*, 1293–1314.

[2] For reviews, see: a) S. Gaillard, J.-L. Renaud, *ChemSusChem* **2008**, *1*, 505–509; b) R. H. Morris, *Chem. Soc. Rev.* **2009**, *38*, 2282–2291; c) M. Zhang, A. Zhang, *Appl. Organomet. Chem.* **2010**, *24*, 751–757; d) K. Junge, K. Schröder, M. Beller, *Chem. Commun.* **2011**, *47*, 4849–4859; e) B. A. F. Le Bailly, S. P. Thomas, *RSC Adv.* **2011**, *1*, 1435–1445.

[3] a) A. M. Tondreau, J. M. Darmon, B. M. Wile, S. K. Floyd, E. Lobkovsky, P. J. Chirik, *Organometallics* **2009**, *28*, 3928–3940; b) T. Inagaki, L. Thanh Phong, A. Furuta, J.-i. Ito, H. Nishiyama, *Chem. Eur. J.* **2010**, *16*, 3090–3096; c) T. Inagaki, A. Ito, J.-i. Ito, H. Nishiyama, *Angew. Chem. Int. Ed.* **2010**, *49*, 9384–9387; *Angew. Chem.* **2010**, *122*, 9574–9577; d) D. Addis, N. Shaikh, S. Zhou, S. Das, K. Junge, M. Beller, *Chem. Asian J.* **2010**, *5*, 1687–1691; e) V. V. K. M. Kandepi, J. M. S. Cardoso, E. Peris, B. Royo, *Organometallics* **2010**, *29*, 2777–2782; f) J. Yang, D. Tilley, *Angew. Chem. Int. Ed.* **2010**, *49*, 10186–10188; *Angew. Chem.* **2010**, *122*, 10384–10386; g) E. Buitrago, L. Zani, H. Adolfsson, *Appl. Organomet. Chem.* **2011**, *25*, 748–752; h)

F. Jiang, D. Bézier, J.-B. Sortais, C. Darcel, *Adv. Synth. Catal.* **2011**, *353*, 239–244; i) L. C. Misal Castro, D. Bézier, J.-B. Sortais, C. Darcel, *Adv. Synth. Catal.* **2011**, *353*, 1279–1284; j) E. Buitrago, F. Tinnis, H. Adolfsson, *Adv. Synth. Catal.* **2012**, *354*, 217–222; k) T. Hashimoto, S. Urban, R. Hoshino, Y. Ohki, K. Tatsumi, F. Glorius, *Organometallics* **2012**, *31*, 4474–4479; l) C. Grohmann, T. Hashimoto, R. Fröhlich, Y. Ohki, K. Tatsumi, F. Glorius, *Organometallics* **2012**, *31*, 8047–8050; m) L. C. Misal Castro, H. Li, J.-B. Sortais, C. Darcel, *Chem. Commun.* **2012**, *48*, 10514–10516; n) A. J. Ruddy, C. M. Kelly, S. M. Crawford, C. A. Wheaton, O. L. Sydora, B. L. Small, M. Stradiotto, L. Turculet, *Organometallics* **2013**, *32*, 5581–5588; o) R. Lopes, J. M. S. Cardoso, L. Postigo, B. Royo, *Catal. Lett.* **2013**, *143*, 1061–1066; p) S. Wu, X. Li, Z. Xiong, W. Xu, Y. Lu, H. Sun, *Organometallics* **2013**, *32*, 3227–3237; q) K. Junge, B. Wendt, S. Zhou, M. Beller, *Eur. J. Org. Chem.* **2013**, 2061–2065.

[4] a) S. Zhou, K. Junge, D. Addis, S. Das, M. Beller, *Angew. Chem. Int. Ed.* **2009**, *48*, 9507–9510; *Angew. Chem.* **2009**, *121*, 9671–9674; b) Y. Sunada, H. Kawakami, T. Imaoka, Y. Motoyama, H. Nagashima, *Angew. Chem. Int. Ed.* **2009**, *48*, 9511–9514; *Angew. Chem.* **2009**, *121*, 9675–9678; c) S. Das, S. Zhou, D. Addis, S. Enthaler, K. Junge, M. Beller, *Top. Catal.* **2010**, *53*, 979–984; d) H. Tsutsumi, Y. Sunada, H. Nagashima, *Chem. Commun.* **2011**, *47*, 6581–6583; e) D. Bézier, G. T. Venkanna, J.-B. Sortais, C. Darcel, *ChemCatChem* **2011**, *3*, 1747–1750; f) L. C. Misal Castro, J.-B. Sortais, C. Darcel, *Chem. Commun.* **2012**, *48*, 151–153; g) S. Das, B. Wendt, K. Möller, K. Junge, M. Beller, *Angew. Chem. Int. Ed.* **2012**, *51*, 1662–1666; *Angew. Chem.* **2012**, *124*, 1694–1698; h) A. Volkov, E. Buitrago, H. Adolfsson, *Eur. J. Org. Chem.* **2013**, 2066–2070.

[5] J. M. S. Cardoso, B. Royo, *Chem. Commun.* **2012**, *48*, 4944–4946.

[6] A. M. D. Greenhalgh, D. J. Frank, S. P. Thomas, *Adv. Synth. Catal.* **2014**, *356*, 584–590.

[7] a) S. Chunji, L. Zhifang, L. Guoqiao, J. Jianxiong, X. Wendong, C. Xiaojun, Faming, Zhuanli Shenqind, 1880289, **2006**; b) S. Chun-Qi, L. Zhi-Fang, Y. Cheng-Jun, L. Guo-Qiao, Q. Huan-Yu, *Youji Huaxue* **2008**, *28*, 515–520; c) Z. Li, C. Sheng, H. Qiu, Y. Zhang, *Org. Prep. Proced. Int.* **2007**, *39*, 412–415.

[8] Y. Sawama, S. Nagata, Y. Yabe, K. Morita, Y. Monguchi, H. Sajiki, *Chem. Eur. J.* **2012**, *18*, 16608–16611.

[9] a) K. Iwanami, H. Seo, Y. Tobita, T. Oriyama, *Synthesis* **2005**, 183–186; b) K. Iwanami, K. Yano, T. Oriyama, *Chem. Lett.* **2007**, *36*, 38–39.

[10] a) S. Das, Y. Li, K. Junge, M. Beller, *Chem. Commun.* **2012**, *48*, 10742–10744; b) D. Bezier, G. T. Venkana, L. C. Misal Castro, J. Zheng, T. Roisnel, J.-B. Sortais, C. Darcel, *Adv. Synth. Catal.* **2012**, *354*, 1879–1884.

[11] a) R. M. Roberts, A. A. Khalaf, in: *Friedel–Crafts Alkylation Chemistry. A Century of Discovery*, Marcel Dekker, New York, **1984**; b) G. A. Olah, R. Krishnamurti, G. K. S. Prakash, in: *Friedel–Crafts Alkylations in Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon Press, Oxford, UK, **1991**; c) T. Yamamoto, M. Fukumoto, N. Sakaue, T. Furusawa, M. Tashiro, *Synthesis* **1991**, *9*, 699–700; d) M. Bandini, A. Melloni, A. Umani-Ronchi, *Angew. Chem. Int. Ed.* **2004**, *43*, 550–556; *Angew. Chem.* **2004**, *116*, 560–566; e) M. Rueping, B. J. Nachtsheim, *Beilstein J. Org. Chem.* **2010**, *6*; f) G. A. Olah, in: *Friedel–Crafts and Related Reactions*, Wiley Interscience, New York, **1964**; vol. II, part 1; g) K. Weissermeland, H.-J. Arpe, *Industrielle Organische Chemie*, Wiley-VCH, Weinheim, Germany, **1988**.

[12] R. M. Roberts, A. M. EI-Khawaga, K. M. Sweeney, M. F. EI-Zohry, *J. Org. Chem.* **1987**, *52*, 1591–1599.

[13] H. Griepentrog, *Ber. Dtsch. Chem. Ges.* **1886**, *19*, 1876–1877.

[14] a) A. Schaarschmidt, L. Hermann, B. Szemzo, *Ber. Dtsch. Chem. Ges.* **1925**, *58*, 1914–1916; b) S. Saito, T. Ohwada, K. Shudo, *J. Am. Chem. Soc.* **1995**, *117*, 11081–11084.

[15] a) K. Mertins, I. Iovel, K. Kischel, A. Zapf, M. Beller, *Angew. Chem. Int. Ed.* **2005**, *44*, 238–242; *Angew. Chem.* **2005**, *117*, 242–246; b) K. Mertins, I. Iovel, K. Kischel, A. Zapf, M. Beller, *Angew. Chem. Int. Ed.* **2005**, *44*, 3913–3917; *Angew. Chem.* **2005**, *117*, 3981–3985; c) K. Mertins, I. Iovel, K. Kischel, A. Zapf, M. Beller, *Adv. Synth. Catal.* **2006**, *348*, 691–695; d) J. Gao, J.-Q. Wang, Q.-W. Song, L.-N. He, *Green Chem.* **2011**, *13*, 1182–1186; e) Y. Sawama, Y. Shishido, T. Kawajiri, R. Goto, Y. Monguchi, H. Sajiki, *Chem. Eur. J.* **2014**, *20*, 510–516.

[16] a) J. Kischel, I. Jovel, K. Mertins, A. Zapf, M. Beller, *Org. Lett.* **2006**, *8*, 19–22; b) M. Rueping, B. J. Nachtsheim, T. Scheidt, *Org. Lett.* **2006**, *8*, 3717–3719; c) H.-B. Sun, B. Li, R. Hua, Y. Yin, *Eur. J. Org. Chem.* **2006**, 4231–4236; d) C.-M. Chu, W.-J. Huang, J.-T. Liu, C.-F. Yao, *Tetrahedron Lett.* **2007**, *48*, 6881–6885.

[17] a) M. H. C. de la Cruz, J. F. C. da Silva, E. R. Lachter, *Appl. Catal. A* **2003**, *245*, 377–382; b) Y. Nishibayashi, Y. Inada, M. Yoshikawa, M. Hidai, S. Uemura, *Angew. Chem. Int. Ed.* **2003**, *42*, 1495–1498; *Angew. Chem.* **2003**, *115*, 1533–1536; c) W.-B. Yi, C. Cai, *J. Fluorine Chem.* **2005**, *126*, 831–833; d) K. Mantri, K. Komura, Y. Kubota, Y. Sugi, *J. Mol. Catal. A* **2005**, *236*, 168–175; e) J. Choudhury, S. Podder, S. Roy, *J. Am. Chem. Soc.* **2005**, *127*, 6162–6163; f) V. D. Sarca, K. K. Laali, *Green Chem.* **2006**, *8*, 615–620; g) M. Rueping, B. J. Nachtsheim, W. Ieawsuwan, *Adv. Synth. Catal.* **2006**, *348*, 1033–1037; h) H.-B. Sun, B. Li, S. Chen, J. Li, R. Hua, *Tetrahedron* **2007**, *63*, 10185–10188; i) S. Podder, J. Choudhury, S. Roy, *J. Org. Chem.* **2007**, *72*, 3139–3132; j) J. R. Satam, R. V. Jayaram, *Catal. Commun.* **2008**, *9*, 1937–1940; k) F. Wang, W. Ueda, *Chem. Eur. J.* **2009**, *15*, 742–753; l) A. Prades, R. Corberán, M. Poyatos, E. Peris, *Chem. Eur. J.* **2009**, *15*, 4610–4613; m) M. M. Khodaei, E. Nazari, *Tetrahedron Lett.* **2012**, *53*, 5131–5135; n) X. Pan, M. Li, Y. Gu, *Chem. Asian J.* **2014**, *9*, 268–274.

[18] X.-K. Guo, D.-Y. Zhao, J.-H. Li, X.-G. Zhang, C.-L. Deng, R.-Y. Tang, *Synlett* **2012**, *23*, 627–631.

[19] a) Y. Hashimoto, K. Hirata, N. Kihara, M. Hasegawa, K. Saigo, *Tetrahedron Lett.* **1992**, *33*, 6351–6354; b) Y. Hashimoto, K. Hirata, H. Kagoshima, N. Kihara, M. Hasegawa, K. Saigo, *Tetrahedron* **1993**, *49*, 5969–5978.

[20] S. Fukuzawa, T. Tsuchimoto, T. Hiyama, *J. Org. Chem.* **1997**, *62*, 151–156.

[21] a) T. Tsuchimoto, T. Hiyama, S.-I. Fukuzawa, *Chem. Commun.* **1996**, *20*, 2345–2346; b) T. Tsuchimoto, K. Tobita, T. Hiyama, S.-I. Fukuzawa, *J. Org. Chem.* **1997**, *62*, 6997–7005.

[22] a) T. Miyai, Y. Onishi, A. Baba, *Tetrahedron Lett.* **1998**, *39*, 6291–6294; b) T. Miyai, Y. Onishi, A. Baba, *Tetrahedron* **1999**, *55*, 1017–1026; c) A. Baba, Jpn. Kokai Tokkyo Koho, JP 2000007590, **2000**; d) Y. Makoto, *Yuki Gosei Kagaku Kyokaishi* **2007**, *65*, 99–108.

[23] N. Sakai, K. Kawana, R. Ikeda, Y. Nakaike, T. Konakahara, *Eur. J. Org. Chem.* **2011**, 3178–3183.

[24] Z. Li, C. Yang, H. Zheng, H. Qiu, H. Lai, *Youji Huaxue* **2009**, *29*, 403–408.

[25] R. Savela, W. Zawartka, R. Leino, *Organometallics* **2012**, *31*, 3199–3206.

[26] Y. Onishi, D. Ogawa, M. Yasuda, A. Baba, *J. Am. Chem. Soc.* **2002**, *124*, 13690–13691.

[27] S.-S. Weng, *Tetrahedron Lett.* **2009**, *50*, 6414–6417.

[28] H. Duan, L. Meng, D. Bao, H. Zhang, Y. Li, A. Lei, *Angew. Chem. Int. Ed.* **2010**, *49*, 6387–6390; *Angew. Chem.* **2010**, *122*, 6531–6534.

[29] H.-B. Sun, B. Li, R. Hua, Y. Yin, *Eur. J. Org. Chem.* **2006**, 4231–4236.

[30] C.-M. Chu, W.-J. Huang, J.-T. Liu, C.-F. Yao, *Tetrahedron Lett.* **2007**, *48*, 6881–6885.

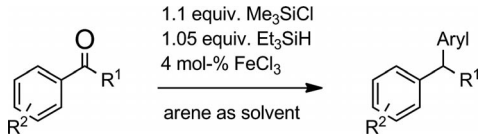
[31] F. G. Bordwell, G. E. Drucker, G. J. McCollum, *J. Org. Chem.* **1982**, *47*, 2504–2510.

[32] a) D. Das, S. Pratihar, S. Roy, *Org. Lett.* **2012**, *14*, 4870–4873; b) N. Akiko, S. Sogo, F. Shizuo, H. Shoji, *Nippon Kagaku Kaishi* **1984**, *4*, 574–579.

[33] a) M. B. Sassaman, K. D. Kotian, G. K. Surya Prakash, G. A. Olah, *J. Org. Chem.* **1987**, *52*, 4314–4319; b) T. Tsunoda, M. Suzuki, R. Noyori, *Tetrahedron Lett.* **1979**, *20*, 4679.
[34] Z. Li, Z. Duan, J. Kang, H. Wang, L. Yu, Y. Wu, *Tetrahedron* **2008**, *64*, 1924–1930.
[35] M. Peña-López, M. Ayán-Varela, L. A. Sarandeses, J. P. Sestola, *Chem. Eur. J.* **2010**, *16*, 9905–9909.
[36] G. Sun, Z. Wang, *Tetrahedron Lett.* **2008**, *49*, 4929–4932.
[37] N. Henry, C. Enguehard-Gueiffier, I. Thery, A. Gueiffier, *Eur. J. Org. Chem.* **2008**, 4824–4827.
[38] M. J. Burns, A. R. Kapdi, I. J. S. Fairlamb, P. Sehnal, R. J. K. Taylor, *Org. Lett.* **2007**, *9*, 5397–5400.
[39] a) D. Srimani, A. Bej, A. Sarkar, *J. Org. Chem.* **2010**, *75*, 4296–4299; b) C.-B. Kim, H. Jo, B.-K. Ahn, C. K. Kim, K. Park, *J. Org. Chem.* **2009**, *74*, 9566–9569.
[40] C.-R. Chen, S. Zhou, D. B. Biradar, H.-M. Gau, *Adv. Synth. Catal.* **2010**, *352*, 1718–1727.
[41] P. Thirupathi, S. S. Kim, *J. Org. Chem.* **2010**, *75*, 5240–5249.
[42] V. Nair, K. G. Abhilash, N. Vidya, *Org. Lett.* **2005**, *7*, 5857–5859.

Received: February 6, 2014
Published Online: ■

Iron Catalyzed Reactions



A robust one-pot, iron-catalyzed chlorination Friedel–Crafts alkylation reaction of benzylic carbonyl compounds, mediated by chlorotrimethylsilane and triethylsilane, has been developed to yield substituted diaryl and triaryl building blocks.

R. Savela, M. Majewski, R. Leino* 1–12

Iron-Catalyzed Arylation of Aromatic Ketones and Aldehydes Mediated by Organosilanes

Keywords: Synthetic methods / Homogeneous catalysis / Iron / Silanes

